Pathology and Etiology.—It is now conceded that boils are due to the entrance of pus cocci (staphylococcus aureus or albus) into the openings of skin glands or hair follicles. According to the researches of Bockhardt,* if the micro-organisms do not penetrate into the cutis, simple impetigo results; if they pass vaguely into the cutis through some lesion in the epidermis, a skin abscess will occur; but if they pass along the duct of a sweat gland or penetrate the lumen of a hair follicle, the process of suppuration is more acute and a furuncle results, the suppurating gland or duct representing the core. Direct inoculation or experimental cultures show conclusively the contagious nature of boils, as was pointed out long ago by Startin. According to Melsome,† it is not possible to obtain cultures in the œdematous area surrounding a boil; however, when a furuncle is large, or is rapidly followed by others in its immediate vicinity, the pus cocci pass through the abscess walls and travel along the lymphatics, producing swelling of the lymph glands, and in severe cases they may even gain access to the general circulation and induce septicæmia.

It is said that women are less subject to boils than men, and that while boils are not uncommon in infants, they are most frequent in boys and young men. Solitary boils are often found to be due to some local irritation, *e.g.*, chafing of rough or frayed garments, decubitus, etc., the irritated skin more readily allowing the penetration of pus organisms. A condition of furunculosis of the back of the neck is not infrequent as the result of infection from the fingers of barbers and the use of the dirty implements of their trade.

Sweaters and other garments worn by young men in training and in athletic games frequently become infected and give rise to boils in otherwise singularly healthy persons.

It is a matter of common experience that furuncles complicate many disorders of a depressing character, *e.g.*, diabetes, variola, typhoid fever, etc. Severe pruritic diseases are also often complicated or followed by boils; for example, eczema in children. In the hot summers experienced in this country the very frequent prickly heat is frequently followed by boils, both in children and adults.

The condition known as furunculosis, or recurrence of boils in crops, is due to local reinoculation and not to the state of the blood, although it is undoubtedly true that the nutrition of the soil will have much to do with the pathogenetic action of the pus cocci.

With our present knowledge of the pathology of boils it may be readily understood how boils sometimes occur quasi-epidemically in families and schools.

Diagnosis.—A boil is to be distinguished from a carbuncle by its conical shape and its single suppurating point; a carbuncle, on the other hand, is larger and flatter than a boil, has several openings, and is surrounded by a much more brawny induration. The difference really is one of degree, the carbuncle being, however, clinically, a much more formidable affection.

Treatment.—In all cases, especially when the eruption has existed for a long time, it is advisable, in addition to the local measures presently to be described, to look into the hygienic surroundings and general health of the patient. The urine should be examined for albumin and sugar, and if these are discovered the proper treatment for those conditions should at once be adopted. All local sources of irritation and possible infection should be diligently sought and removed. Old smoking jackets, sweaters, etc., should be regarded with suspicion. A proper disinfection of barber's tools should be insisted upon.

Now that the specific character of the furuncle is better understood there is less insistence upon the administration of the host of remedies that are supposed to be "good for boils."

Among such remedies may be mentioned yeast in doses of a half-wineglassful morning and night, and the sulphide of calcium so highly praised by Ringer. It is quite possible that the sulphide of calcium may possess some germicidal properties, but it must be given in much larger doses than those usually recommended. Dilute sulphuric acid in ten to twenty drop doses, well diluted, every three or four hours, is highly esteemed by some physicians. Medicines that improve the general nutrition, thus rendering the individual less susceptible to local infection, are of undoubted value in furunculosis; for example, iron, arsenic, cod-liver oil, the hypophosphites, and the syrup of the lacto-phosphate of lime may be prescribed with hope of benefit in suitable cases.

As regards the direct treatment of the boil itself an effort should be made to prevent if possible, or at least limit, the suppuration. Very often a boil may be aborted by the application of a salicylic acid plaster, as after L. Heitzmann's formula:

℞ Acidi salicylici .... ʒ ij.
Emplastri saponis .... ℥ ij.
Emplastri diachyli .... ℥ i.
M. S. Spread on cloth.

Other remedies of this class are iodine, boric acid in saturated solution, and ichthyol. Halle and Jamieson advise the following application:

℞
Tincturæ iodi.................... ʒ i.
Acidi tannici .... ʒ ss.
Pulveris acaciæ.................... ʒ ss.

A few drops of carbolic acid injected into the apex of a boil will often cause it to abort. An electrolytic needle will do the same thing. If a hair occupies the centre of a furuncle it is best to extract it.

Unna's mercuric-carbolic plaster often succeeds in aborting a boil; but if suppuration has already begun, nothing succeeds so well in hastening it. A hole should be cut in the centre of the plaster corresponding to the apex of the boil. When boils are very painful the common practice is to apply a hot flaxseed poultice, but unless it is rendered antiseptic by the addition of carbolic acid it is apt to prove mischievous by favoring reinfection in the vicinity. The following ointment serves all the purposes of a poultice, does not encourage reinfection, and allays pain most decidedly:

℞ Pulveris iodoformi .... ʒ i.
Unguenti vaselini plumbici............ ℥ i.
M. S. Spread on patent lint.

If the patient exhibits any idiosyncrasy in regard to iodoform, aristol or xeroform may be used in its place.

The internal administration of appropriate doses of phenacetine will usually secure sleep at night. If incisions are imperatively demanded the parts may be rendered insensible by a spray of ethyl chloride. It is an absolute necessity, especially where boils are multiple, to smear the intervening and surrounding skin with a paste made of equal parts of oxide of zinc and vaseline and four-per-cent. boric acid. Washing the skin with green soap and warm water and mopping on a solution of bichloride of mercury 1 to 1,000 often puts a stop to reinoculation. Clean underclothes should be put on frequently and the patient warned against carrying infection to other parts with his fingers. Squeezing and other manipulation of a boil should be avoided. After the boil has burst the resulting cavity should be treated on ordinary surgical principles.

W. A. Hardaway.

* Monatshefte für Derm., No. 10, 1887.
† Allbutt's System of Medicine, vol. i., 1896.

BOLDO.—The leaves of *Peumus Boldus* Molino (fam. *Monimiaceæ*). This is a large, much-branched shrub or small tree of Chile, evergreen and highly aromatic, the leaves opposite, the flowers small, white, panicled, diœcious. The leaves usually dry of a brownish color. They are coriaceous and very thick, ovate or oval-ovate, blunt or emarginate, entire, rough, papillose and stellate-hairy. They contain numerous large oil vesicles, and have a strong, somewhat turpentine-like odor and an aromatic, burning taste.

Boldo contains about two per cent. of a powerful volatile oil, with resin, a little tannin, three per cent. of the glucoside boldin, and one-tenth per cent. of the alkaloid boldine. The statements concerning the properties of the constituents are very discordant. According to Merck, the hepatic properties reside in the glucoside, the dose of which is 0.065 to 0.2 gm. (gr. i. to iij.), and the hypnotic properties in the alkaloid, the dose of which is 0.002 to 0.0065 gm. (gr. $\frac{1}{30}$ to $\frac{1}{10}$).

The properties of the leaves are very marked, and it seems strange that the drug should not have acquired a higher repute. Its original use was that of an alterative, with special reference to the liver. Marked sedative properties were encountered, and it has been considerably used as a hypnotic in insomnia. For the latter purpose the dose should be 2 to 4 gm. (ʒ ss. to i.), for the former a fourth as much. The drug should be systematically investigated. It is now very little used.

H. H. Rusby.

BONDUC.—*Bonduc Nut; Nicker Tree.*

The seeds of *Cæsalpinia Bonducella* (L.) Roxb. and of *C. Bonduc* Roxb. (fam. *Leguminosæ*).

These plants are not only abundant in India, where they are native, but have been very largely introduced to most tropical countries. The seeds have the shape of a smooth pea, but are one-half or three-fourths inch in diameter, and smooth and shining. Those of the *C. Bonducella* are of a peculiar gray lead-color, those of *C. Bonduc* yellowish brown. The former especially are classical in the medical history of India, the uses being numerous and varied, and some of them doubtless ignorant. Its chief reputation appears to have been in the treatment of malaria, and careful trial has shown it to possess antiperiodic properties of some importance. The seeds contain twenty-five per cent. of fixed oil, which has been expressed and used like other fixed oils. They also contain about two per cent. of an amaroid, which is a white powder, and apparently the active constituent. Like all seeds of their class, they are rich in protein. The shell contains tannin. The antiperiodic dose of the bitter principle is 0.1 to 0.2 gm. (gr. iss. to iij.).

H. H. Rusby.

BONE. (HISTOLOGY.)—Bone tissue is closely allied in genesis and in many of its structural features to the other members of the connective-tissue group, the most evident difference between it and other tissues of the same class consisting in the solidity and firmness of the basement substance. For in this, as in other connective tissues, we have to consider the cells and the basement substance and the way in which they are arranged to form the different varieties of tissue. The solidity of the basement substance of bone depends largely upon the deposition within it of calcium phosphate and carbonate, with small amounts of calcium fluoride, sodium chloride, and salts of magnesium. These inorganic salts, which form about two-thirds of the weight of the bone, are deposited in an organic matrix in such a condition of minuteness that they are not recognizable as particles even with high powers of the microscope. They may be dissolved out of the bone with dilute acids, leaving a translucent flexible material behind, which preserves the shape and general structural features of the bone.

The soft matrix which is left, after the extraction of its inorganic salts, may be converted into gelatin by boiling in water. It is sometimes called the cartilage of bone, or ossein; but there is no sufficient reason for using these names, since the matrix is really, both in chemical nature and in minute structure, closely allied to the basement substance of fibrillar connective tissue.

The varied gross appearances which different bones or different parts of the same bone present have given rise to the names *compact bone tissue* and *cancellous bone tissue* or *spongy bone*. But the essential structure of the tissue is the same in both, the difference consisting largely in the arrangement of the bone tissue proper, and its abundance in proportion to the marrow spaces or vascular canals which it encloses. The compact bone tissue is in general found in the outer portions of the bones, while the cancellous tissue is situated internally, either entirely filling the central portions or bordering the marrow cavities.

Bones are surrounded by a layer of vascular connective tissue called the *periosteum*, and contain, either in large central cavities or in the smaller spaces with which they are everywhere permeated, a delicate vascular tissue called *marrow*. We have, then, to consider: 1. bone tissue proper; 2. the periosteum; 3. the marrow.

1. *Bone Tissue Proper.*—If we remove the inorganic salts from one of the long bones, by soaking it in dilute chromic or picric acid (see article on *Histological Technique*), and then make a thin longitudinal section, microscopical examination with a low power of these sections, stained with eosin and mounted in glycerin, reveals a picture like that represented in Fig. 638. The more solid portions of the bone show a series of narrow canals, running in a direction in general parallel with the long axis of the bone, and in frequent communication with one another by similar short transverse or oblique canals. These are the so-called *Haversian canals*, and contain blood-vessels, and, depending upon their size, few or many variously shaped cells. Along these Haversian canals the basement substance will be seen arranged in a series of lamellæ, while in and between these lamellæ lie small, elongated cavities called lacunæ, in which are the bone cells. Transverse sections, however, through the middle of a long bone, reveal with more distinctness the arrangement of the lamellæ of the basement substance (Fig. 639). The Haversian canals, which are cut transversely or obliquely across, are surrounded by a series of concentric lamellæ. These Haversian lamellæ, with their enclosed lacunæ, together with the canals and their contents, form the so-called *Haversian systems*. Filling the larger and smaller irregular areas between the Haversian systems are other parallel lamellæ, which run in various directions, and which are called *intermediary systems*. Beneath the periosteum, at the external surface of the bone, is a thinner or thicker system of lamellæ called *circumferential* or *general lamellæ*, which cover over large numbers of the Haversian systems and surround the entire bone. Sometimes similar but less well-defined general systems of lamellæ border the marrow cavity, but more often the internal surface of the compact bone is beset with a series of projecting bony trabeculæ, consisting of lamellæ similar to those forming the systems of the compact bone, and inclosing large, irregular spaces. This is the cancellous tissue bordering the marrow cavity. In the heads of long bones, and in

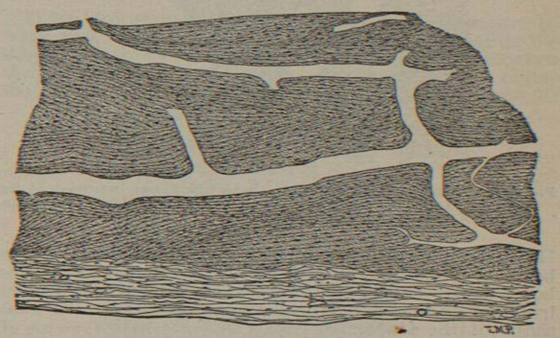

Fig. 638.—Longitudinal Section of Human Tibia, Decalcified and Mounted in Glycerin. (× about 20 and reduced.)

most short or irregular-shaped bones the cancellous tissue occupies the entire central portion.

If, now, we study more closely the minute structural features of the bone, we find in the first place that the

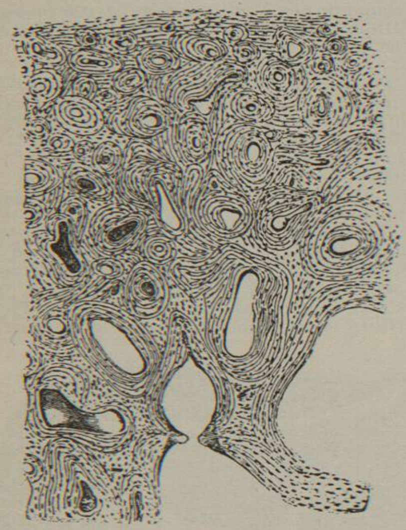

FIG. 639.—Transverse Section of a Bone (the Ulna) Deprived of Its Earth by Acid. (Sharpey.) Magnified 20 diameters. Haversian systems of canals and concentric lamellæ.

Haversian canals, as seen in transverse sections of the bone, vary considerably in size and shape. Some are large, others small; some are round, others oval, others irregular in shape. In many cases, however, the oval shape of the Haversian canals and of their systems of

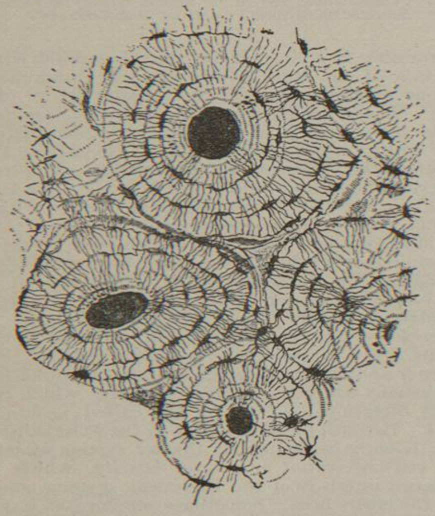

FIG. 640.—Transverse Section of Compact Tissue of Humerus. Magnified about 150 diameters and then slightly reduced. (Sharpey.) Three of the Haversian canals are seen, with their concentric rings; also the lacunæ, with the canaliculi extending from them across the direction of the lamellæ. The Haversian apertures had become filled with air and débris (from the grinding), and therefore appear black in the figure, which represents the object as viewed with transmitted light.

lamellæ appears to be due to the obliquity of the section. In some cases the canals lie in the centre of the systems, in others near the side. Sometimes the Haversian systems are complex, one set of concentric lamellæ seeming to have encroached upon the space formerly occupied by another (Fig. 639). Furthermore, the borders of many of the Haversian systems, where these abut on one another or upon the intermediary systems, appear scolloped or jagged. This appearance will be explained below, when we consider the growth of the bone.

Turning now to the bone cells and the spaces in which they lie—the lacunæ—we find that some other mode of preparation is necessary than that of mounting sections of decalcified bone in glycerin, because the whole extent of the cell spaces is not revealed, on account of their partial filling by the mounting medium.

If, however, we take a bone which has been macerated and dried, to remove the fat and other soft tissues, and prepare thin sections by grinding and polishing them, and then mount them in hard balsam, which is melted, and, after the section is enclosed, cooled so quickly that it does not have time to penetrate far into the tissue, the full extent of the cell cavities is revealed. For all the spaces are now filled with air, which gives them a dark appearance by transmitted light. In a section thus pre-

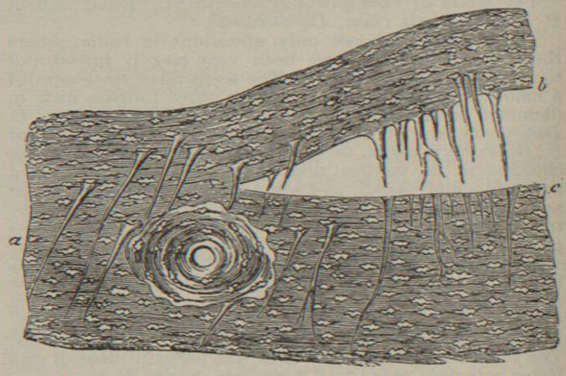

FIG. 641.—Section through the External Table of a Decalcified Human Parietal Bone. *a*, Sharpey's fibres in their natural position; *b*, fibres which have been pulled out of the underlying basement substance, *c*. (After H. Müller.)

pared (Fig. 640), it will be seen that the lacunæ are elongated, mostly fusiform, irregular cavities, lying between and in the lamellæ, and that from these minute branching canals, called *canaliculi*, pass off, piercing the lamellæ and forming frequent communications with the canaliculi of neighboring lacunæ. The canaliculi which pass out from the lacunæ lying near the Haversian canals pierce the walls of the latter and open into them. The canaliculi of neighboring Haversian systems, however, do not, as a rule, communicate with one another.

In the lacunæ, as may be seen in carefully prepared thin sections of decalcified bone, lie the flattened and, in some cases, branching bone cells. To what extent the branches of the cells pass into the canaliculi is not yet fully established. The bone cells have large nuclei and finely granular bodies.

According to von Ebener, Sharpey, and others, the basement substance of bone is not homogeneous, but is permeated by exceedingly minute decussating fibrils, similar to those of the basement substance of ordinary fibrillar connective tissue. Certain of the lamellæ, particularly those of the circumferential and intermediary systems, are pierced by bundles of delicate fibrils, which pass perpendicularly or obliquely through them. These fibre bundles, called *Sharpey's fibres*, may be seen projecting from the inner side of small bits of bone torn forcibly away from one another, near the surfaces of decalcified bones (Fig. 641) as well as in very thin sections. These

Sharpey's fibres, as will be seen when we come to the development of bone, are the remains of the old fibrillar connective-tissue matrix in which the bone is formed.

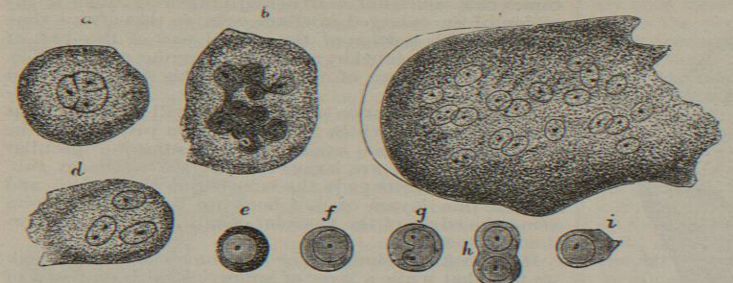

FIG. 642.—Cells of the Red Marrow of the Guinea-Pig. Highly magnified. (Schäfer.) *a*, A large cell the nucleus of which appears to be partly divided into three by constrictions; *b*, a cell the enlarged nucleus of which shows an appearance of budding into a number of smaller nuclei; *c*, a so-called giant cell or myeloplaxe with many nuclei; *d*, a smaller myeloplaxe with three nuclei; *e–i*, proper cells of the marrow.

2. *The Periosteum* is a fibrous sheath surrounding the bones, except over their articular surfaces. It consists of moderately dense layers of fibrillar connective tissue containing numerous blood-vessels, which ramify in the outer portions and finally enter the bone through the Haversian canals. There is a considerable number of elastic fibres in the inner portions of the periosteum, and it contains an abundant system of lymphatic vessels. In the growing bone irregular layers of large granular cells, called osteoblasts, lie in the inner layers of the periosteum, and between it and the bone. The periosteum contains a few nerves, which chiefly pass from it into the bone tissue.

3. *The Marrow* is a complex tissue which fills the large central cavities in the shafts of the long bones, the spaces in the cancellous tissue, and the larger Haversian canals. Marrow tissue varies considerably in its appearance and structure in adults and in the young, as well as in different bones in the adult. In the adult the marrow in the shafts of long bones consists of blood-vessels and a delicate connective-tissue reticulum which supports a great abundance of fat cells and a varying number of small spheroidal cells scattered between the fat cells. Such marrow has a yellow appearance from the fat which it contains. In the cancellous tissue of both long, irregular-shaped, and short bones in the adult, and in all of the bones in young animals, the marrow is red in color, and contains comparatively few fat-cells. Red marrow consists, like the yellow marrow, of blood-vessels, lymph vessels, and a delicate reticular framework whose meshes are more or less filled with cells. These cells are of several kinds (see Fig. 642). There are abundant small spheroidal cells with nuclei, which are very large in proportion to the size of the cell body; and between these and considerably larger cells, also with large and often irregularly shaped and sometimes double nuclei, there are numerous intermediate forms. All of the above forms are very abundant in red marrow, and constitute the *marrow cells* proper (Fig. 642). Then we find, much less frequently, and in varying numbers in different bones of the same animal, and in the bones of different animals, much larger, usually multinucleated cells, the so-called *myeloplaxes* or giant cells (Fig. 642). These myeloplaxes, although always large, vary considerably in size and shape, and in the number of their nuceli. The nuclei are apt to be collected in a compact mass near the centre of the cell, and often present quite bizarre and indescribable shapes. Finally, red marrow contains, in varying number, small nucleated cells, which bodies have the color and general appearance of red blood cells, the so-called *nucleated red blood cells*, and small spheroidal cells whose bodies contain larger and smaller particles of pigment, and a moderate number of fat cells.

THE DEVELOPMENT OF BONE.—It will be possible within the limits of this article to give only a very brief general description of the somewhat complex way in which bone is formed. It is customary to describe the development of bone as occurring in three ways, or, speaking more correctly, to describe three phases of bone development. These are *intracartilaginous, intramembranous,* and *subperiosteal.* It should be borne in mind, however, that the essential nature of the process is the same in all.

Intracartilaginous Ossification.—Most of the long and irregular-shaped bones in the body consist, at an early period of life, of masses of hyaline cartilage, which present, in a general way, the shape of the future bone. The transformation of these cartilage masses into bones is intracartilaginous ossification. This is always associated with a certain amount of subperiosteal ossification in the manner to be described below.

If we look at one of the cartilage masses which is to be converted into a long bone—at one of the bones of the finger or toe, for example (Fig. 643)—at a period when the process of ossification is about to commence, we notice that at the central portion of the mass the cartilage cells

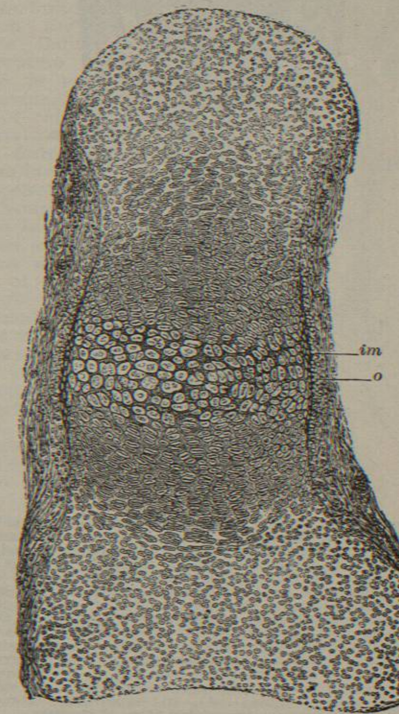

FIG. 643.—Section of Phalangeal Bone of Human Fœtus, at the Time of Commencing Ossification. (Schäfer.) The cartilage cells in the centre are enlarged and separated from one another by dark-looking calcified matrix; *im*, layer of bone deposited underneath the periosteum; *o*, layer of osteoblasts by which this layer has been formed. Some of the osteoblasts are already embedded in the new bone as lacunæ. The cartilage cells are becoming enlarged and flattened and arrayed in rows above and below the calcified centre. At the ends of the cartilage the cells are small and the groups are irregularly arranged; the fibrous periosteum is not sharply marked off from the cartilage.

are larger (Fig. 643) than in other parts, and closer together, and that the basement substance between them is finely granular from the deposition in it of salts of lime.

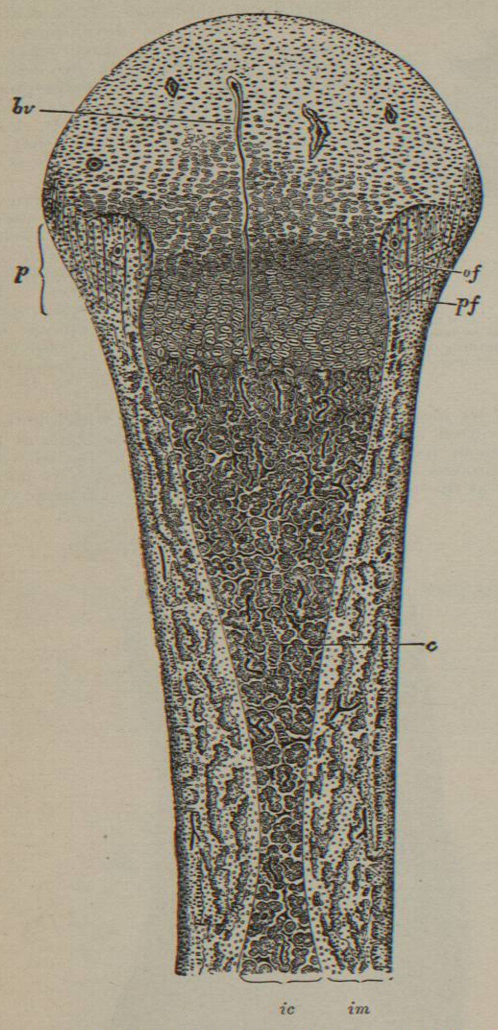

FIG. 644.—Longitudinal Section through the Upper Half of the Decalcified Humerus of a Fetal Sheep. Magnified about 30 diameters. (Schäfer.) *ic*, The part of the shaft which was primarily ossified in cartilage. One long, straight vessel (*bv*) passes in advance of the line of ossification far into the cartilaginous head; most of the others loop round close to the cartilage. At one or two places in the older parts of the bone, elongated groups of cartilage cells (*c*) may still be seen which have as yet escaped absorption; *im*, the part of the bone that has been ossified in membrane, that is to say, in the osteoblastic tissue under the periosteum. The subperiosteal layer is prolonged above into the thickening (*p*), which encroaches upon the cartilage of the head of the bone, and in which are seen, among numerous osteoblasts and a few blood-vessels, the straight, longitudinal osteogenic fibres (*of*), and some other fibres (*pf*) crossing them, and perhaps representing fibres of Sharpey.

While this preliminary calcification of the cartilage and the enlargement of its cells is going on, a shell of bone is forming around the middle of the shaft beneath the periosteum, and as the cartilage near the ends continues to grow and expand at the sides, the entire mass assumes somewhat of an hour-glass shape. Now the blood-vessels from the perichondrium—which has become a periosteum on account of the above-mentioned shell of bone which has been formed around the shaft—begin to advance in the central portion of the cartilage, and this becomes channelled out in irregular branching canals in the region of the enlarged cartilage cells, so that after a time a considerable portion of the central part of the shaft of the bone is permeated by a series of vascular canals. The general appearance of the bone at this time is seen in Fig. 644.

A closer examination at this period will show: (1) that the cartilage cells which lie in the region just beyond the advancing vascular canals have assumed a peculiar arrangement and are large; (2) that the basement substance of the cartilage in the same region is calcified; and (3) that thin layers of new bone are beginning to form along the edges of the vascular canals in the central portion of the shaft.

If we look at a similar bone at a somewhat later period, we find that while a layer of subperiosteal bone tissue of considerable thickness has been formed round the shaft, the central portions of the structure are also filled with irregular bony trabeculæ, between which lie the vascular canals or marrow cavities (Fig. 644); and, furthermore, that the cartilage cells toward the ends of the bone, in the region just in front of the advancing marrow cavities, are, as before, large and arranged in rows and lie in a calcified basement substance.

It is now necessary to look more closely at the changes in the cartilage which precede the ossification, and to study the exact way in which bone tissue is formed along the walls of the advancing marrow cavities.

If we look with a high power at a thin section of a carefully preserved and decalcified bone in the process of development, confining our attention for a moment chiefly to that region which lies along the ends of the above-described advancing marrow cavities, and for a short distance on either side, we find a condition similar to that represented in Fig. 646. At some distance toward the end of the bone from the medullary cavities the cartilage cells become flattened and are arranged in irregular rows, *b*; nearer the ossifying portions of the bone the cartilage cells are larger and more closely packed together; and finally, just beyond the ends of the advancing marrow canals, large cartilage cells are seen lying in elongated cavities in the basement substance, *c*. Each cavity contains several cells, which, in many cases, are separated from one another by narrow partitions of cartilage basement substance. Here and there along this region it will be seen that the marrow canals with their contained blood-vessels have opened into and become continuous with the spaces containing the large cartilage cells, and the latter have either disappeared or have assumed some different form. This occurs sooner or later, and usually at about the same time, all along this region, so that the advancing blood-vessels convert the spaces originally containing cartilage cells into vascular canals or marrow cavities.

If we look now at the region near the ends of the marrow canals, we find that these canals contain thin-walled blood-vessels, numerous small spheroidal cells, and larger cuboidal, ovoidal, or fusiform granular cells, which are apt to be arranged along the sides of the canals. These latter cells are the so-called *osteoblasts*, under whose influence the bone tissue is formed.

The exact way in which the bone tissue is deposited under the influence of the osteoblasts may be readily seen in very thin sections through the zone of ossification, which have been stained double with hæmatoxylin and eosin (see article on *Histological Technique*) and mounted in balsam. A small portion of such a section made transversely across the bone is represented in Fig. 645. Just beneath the osteoblasts which lie along the edges of the marrow canals thin crescentic shells of strongly refractile calcareous material—the basement substance of bone—are formed. These shells grow thicker and thicker, and rise up around the sides of the osteoblasts. They are pierced by delicate canals, which

are to form the canaliculi. Gradually the entire osteoblast, which has become somewhat flattened and jagged in outline, is enclosed by the bony basement substance and becomes a bone cell. This process goes on around the osteoblasts, which lie side by side all along the walls of the marrow spaces, so that the latter are presently enclosed by an irregular wall or encasement of new bone. Upon this, new layers are deposited, so that gradually the marrow spaces grow narrower and narrower, and finally contain only blood-vessels and a few marrow cells. This gradual bony thickening of the walls and narrowing of the marrow spaces may be seen by following the tissue in a longitudinal section from the line where ossification commences, near the distal ends of the marrow spaces, toward the centre of the bone where the process is oldest.

FIG. 645.—Bony Trabecula from the Lower Jaw of a Calf Embryo, with Howship's foveolæ and giant cells at the ends where absorption is proceeding and osteoblasts covering the sides where bone is being deposited. (Kölliker.)

The fragmentary remains of the old basement substance of the hyaline cartilage persist for some time, surrounded by the new-formed bone; but they grow smaller and smaller as more bone is formed, and are finally absorbed and altogether disappear.

Thus the ossification of the cartilages advances toward their ends, preceded always by a rearrangement and proliferation of the cartilage cells, and by calcification of its basement substance. What the exact purpose is of the temporary calcification of the cartilage basement substance just in advance of the ossification line we do not know, nor is it certain what becomes of the cartilage cells when the vascular canals finally open into the spaces in which they lie. Some observers believe that they disintegrate and are absorbed; others, that they become osteoblasts, or other marrow cells. Equally uncertain is the origin of the osteoblasts, and the consideration of the more or less well-founded conjectures as to their genesis would lead us beyond the scope of this article.

After a time new centres of ossification are formed near the ends of the long bones, in the epiphyses, from which bone formation proceeds in the manner above described. At length the zones of ossification in the epiphyses and diaphyses approach one another, and are separated only by a narrow band of cartilage, which finally itself becomes ossified, and the epiphysis and diaphysis are joined to form a single bone.

Intramembranous and *Subperiosteal Ossification* vary only in details from the intracartilaginous. In the former case, the tissue in which bone is to form is fibrous and vascular; osteoblasts appear along the bundles of fibres which become calcified, and bone is formed around them in the above-described manner. Some of the fibrous bundles persist within the new-formed bone, as Sharpey's fibres. The bone tissue which is at first formed is arranged in irregular trabeculæ, which cross and interlace as did the connective-tissue fibres which it replaces, and encloses irregular vascular spaces or marrow cavities, which become smaller and smaller as successive layers of bone are formed around their sides. After a time the irregular trabeculæ and their enclosed marrow spaces become covered in by more uniform layers of bone. These, in the long bones, are the circumferential lamellæ, and in the flat bones, such as those of the skull, are the compact external and internal tables which enclose the diploë.

A pure intramembranous ossification is seen in the early stages of the formation of the flat bones of the skull. The subperiosteal ossification, on the other hand, occurs as above indicated, simultaneously with the intracartilaginous bone formation in the long bones, as well as at a later stage in the formation of bones which are originally laid down as membranes.

GROWTH OF BONE.—The growth of bones when they are once formed, either in membranes or cartilages or beneath the periosteum, is a somewhat complex process. They increase in thickness by a continued subperiosteal ossification. The increase in length of long bones goes on by the ossification in cartilage until, as above stated, the epiphysis is finally joined to the diaphysis.

The large central marrow cavity of long bones, which in the adult bone is itself much larger than the entire bone at an early stage of development, is formed by the absorption of the earlier developed intracartilaginous and subperiosteal bone. This absorption occurs under the influence of large, irregular-shaped, frequently multinuclear granular cells, called *osteoclasts*. Around these cells, as they lie against the bone tissue, the latter becomes absorbed in some way, so that little pits are formed in which they lie. These pits or depressions, which are of various sizes and shapes, are called *Howship's lacunæ*. On the side of the osteoclasts which lie against the bone there is, according to Kölliker, a shining striated border. The exact nature of the influence by which the osteoclasts induce the absorption of the bone is not well understood.

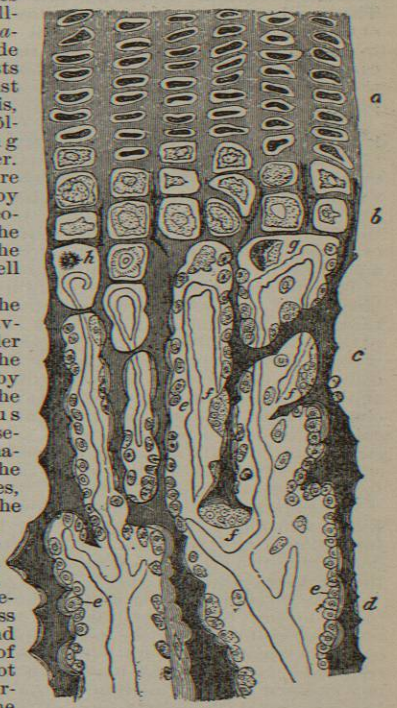

FIG. 646.—Part of a Longitudinal Section of the Developing Femur of the Rabbit. Magnified about 350 diameters. (Klein and Noble Smith.) *a*, Rows of flattened cartilage cells; *b*, greatly enlarged cartilage cells close to the advancing bone, the matrix between being partly calcified; *c*, *d*, already formed bone; the osseous trabeculæ being covered with osteoblasts (*e*), except here and there, where a giant cell or osteoclast (*f*) is seen, eroding parts of the trabeculæ; *g*, *h*, cartilage cells which have become sunken and irregular in shape.

Not only are the central marrow cavities formed under the influence of the osteoclasts, but by an absorption of the bone in various places, and a subsequent new formation of it over the absorbed surfaces, a remodelling of the bone may occur, inducing the various changes in shape which growing bones present. This process of absorption and redeposition of bone goes on, not only on the surfaces, but in the substance, even of compact bone, during early and adult life, inducing the minor changes which occur at this period. The intermediary systems of lamellæ, above described, as seen in transverse sections of long bones (Fig. 646), are, in many cases at least, the remains of older lamellæ which have been partially absorbed; the absorption spaces having been afterward filled in by new Haversian systems. What the conditions are whose fulfilment determines now an absorption and again a new formation of bone, or exactly what the origin of the osteoclasts is, and what their relation to the osteoblasts, we can, in the present state of exact knowledge, do little more than conjecture.

Consult, for the bibliography of the histology, development, and growth of bone, Quain's "Anatomy," vol. i. part ii., tenth edition, and the "Index Catalogue of the Library of the Surgeon-General's Office, U. S. A.," vol. ii.

T. Mitchell Prudden.

BONE. (PATHOLOGICAL.)—Bone, like all tissues, is subject to a continuous waste and repair. New bone is constantly formed and the old absorbed; and while in the adult these processes may be very slight, under the influence of pathological conditions they become very marked; hence the conditions known as pathological apposition, absorption, and transformation of bone. Apposition occurs by the formation of bone from the periosteum. The deeper layers of periosteal cells become converted into large epithelioid cells, the so-called osteoblasts, which later become irregular in shape; the intercellular substance becomes calcified and thus new bone is formed. The new bone may be spread out over the surface of the old, and become firmly attached to it, or it may be limited to a small portion of the surface of the bone. In the first case the process is called hyperostosis and exostosis; in the latter, the processes of new bone are called osteophytes.

Absorption or resorption of bone occurs at the medullary surface and is due to the activity of the large multinucleated cells known as osteoclasts. Occasionally this may occur at the periosteal surface, and we have the surface of the bone becoming irregular and porous—osteoporosis. This occurs occasionally in the very aged, in the bones of the calvarium, as the result of senile atrophy, or it may be secondary to inflammatory exudates, tumors, aneurisms, etc., which exert pressure upon the bone.

Transformation of bone is brought about by a combination of apposition and resorption. By means of these processes the form of bones is changed to meet pathological conditions and changes in function. This is more particularly true of the size and direction of the columns of bone in cancellous structures. If the amount and direction of the load to be borne by the bone become changed, then will the thickness and direction of the columns of bone become changed in the direction of the static demand. By reason of this characteristic of bone, such great artificial deformities are produced as are seen, for instance, in the Chinese foot.

Regeneration of bone is seen following every fracture. Every solution of continuity in bone is followed by the formation of new bone, not only sufficient to replace the defect, but also enough to form a large mass surrounding the fracture (callus).

In fractures of long bones, one differentiates an internal callus formed by the medullary structures, and an external callus formed by the periosteum. This new bone or callus remains intact until the function of the bone is resumed. Later on, that portion of the callus which is not situated in the direction of the load-bearing lines becomes absorbed, and the form of the new bone, just as that of the old, becomes changed to meet the static demands made upon it by the function of the bone—*i.e.*, that of bearing a load.

Osteomalacia is a chronic disease of bone, occurring in adults and most frequently in puerperal women; it is attended by a progressive softening and absorption of bone beginning in the centre and extending outward. The process is followed either by fracture or by deformity of the bones affected. It differs from rachitis in this, that while in the latter we have a deficient deposition of lime salts in newly formed bone, in osteomalacia bone which is already formed is deprived of its earthy material and absorbed. The changes that occur in the bone are not due to any active process on the part of the bone tissue itself. There are no active changes to be discovered in the bone cells. The only thing to be found in the lacunæ is the occasional presence of droplets of fat, which is evidence of a passive destruction of the bone cells.

In the medullary tissue, however, there are to be seen evidences of very marked, active proliferative processes. This is to be observed in the marrow of the long bones, in the medullary tissue of spongy bone, and also in the Haversian canals, which latter normally contain very little medullary tissue. This tissue is the seat of a marked hyperæmia which has converted it into a bright red, succulent tissue, free from fat and extremely rich in proliferating cells. All the medullary tissue seems to have the appearance of the red marrow of infantile bone. This tissue pushes its way outward at the expense of the adjacent bone, first depriving it of its lime salts and later causing its complete absorption.

Thus the compact bone of the diaphysis is converted into spongy bone by the enlargement of its Haversian canals; the trabeculæ of spongy bone are absorbed. If the process continue long enough there remains little of the bone except marrow and periosteum; so that it has been converted into a soft, decalcified, sausage-like mass of marrow, that is held together by the periosteum with perhaps a thin, paper-like layer of bone beneath.

The process may be distributed over a period of several years with occasional cessation. In such an event the medullary tissue loses its signs of active proliferation, the hyperæmia diminishes, and the tissue appears as a yellowish, fatty mass, or as a pale, gelatinous, mucoid, semi-fluid material. In the latter event many of the cells have undergone mucoid degeneration, and if this has been extensive it may have led to the formation of mucoid cysts. This period of quiescence may again give place to a renewed activity as before and to a further destruction of the bone.

This process has a certain resemblance, in activity, to that of inflammation, but the phenomena that attend either acute or chronic inflammation of bone are never present. We never find either suppuration or the formation of new bone.

The cause of decalcification of bone in this disease has been sought for chemically. Some investigators have found an excess of lactic acid in affected bones, and also in the urine, and the solvent action of this acid has been brought forward as the chemical agent which brings on decalcification. Other observers have failed to find this excess. The amount of gluten is diminished in the bones affected. There has been found in the urine a peculiar albuminous substance supposed to be derived from the organic substance of bone.

The bones of the pelvis and of the spinal column are most frequently affected, then come those of the thorax, and of the lower and upper extremities. The bones of the head are very rarely the seat of the disease; the teeth are never involved.

In the non-puerperal cases, the predisposing causes are malnutrition and living in dark, damp houses.

Osteomalacia has been observed in animals who are badly fed and stabled in dark, damp places.

Osteomalacia is a comparatively rare disease. It is rarely seen in England and America; it is more frequent in Germany than in France. In some parts of Germany the disease is more frequent than in others; thus in the Rhine valley and in Southern Germany the disease is more common than in other districts.

The preponderance of puerperal females affected is very striking. Thus of one hundred and thirty-one cases gathered together in the report of Letzmann, in 1861, eighty-five were in women who became ill either during pregnancy or during the puerperal period. Repeated pregnancy and prolonged nursing in poorly nourished women predispose to the disease.

In all of these puerperal cases the disease began in the bones of the pelvis, and in many it was limited to that region. It is therefore highly probable that the great circulatory changes in the pelvis attending pregnancy have a decided influence on the causation of the disease. Fehleisen regards the disease as a reflex trophoneurosis of the blood-vessels of bone, causing a dilatation and proliferation of the marrow at the expense of the bone, and having its origin in the ovaries. The removal of the

ovaries has been practised as a curative measure with some, though not universal success.

Of forty-six non-puerperal cases, thirty-five were in women and eleven in men. These cases are, as a rule, more rare than the puerperal.

Rachitis or *rickets* is a disease occurring in children. It is caused by improper food and bad hygienic surround-

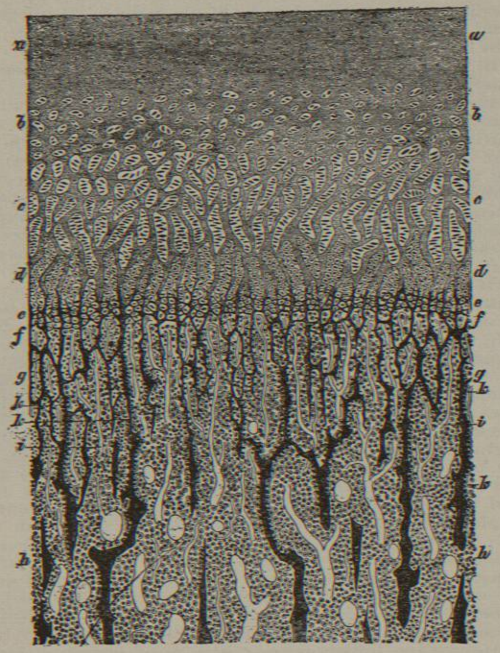

Fig. 647.—Section through the Line of Ossification of a Normal Femur from a Healthy Child. *a*, Hyaline cartilage; *b*, zone in which the cartilage cells are hypertrophied; *c*, cells arranged in columns; *d*, columns of hypertrophic cartilage; *e*, zone of temporary calcification; *f*, zone showing beginning of medulla; *g*, first bony formation; *h*, spongy bone; *i*, blood-vessels; *k*, osteoblasts. (After Ziegler.)

ings, and is attended by a disturbance in growing bone whereby the reabsorption of bone is increased, the calcification of incompletely formed bone is diminished, and the formation of so-called osteoid tissue is excessive. It has been aptly and briefly described by Jenner as "an increased preparation for ossification but an incomplete performance of the process." The disease is most marked in the epiphyses of long bones and the margins of flat bones.

During the formation of normal, healthy bone there is always going on an absorption of already formed bone, which, however, remains confined to certain limits. In rickets the extent of this reabsorption is increased, so that in severe cases a large part of the bone may disappear. As a result, in the long bones the cortical layer becomes more or less osteoporous, and the columns of bone in the spongy portions become thinner and many of them disappear. This reabsorption of bone is lacunar, and, as in the case of normal bone, is due to the action of osteoclasts.

The most striking change is that which occurs in the epiphyseal ends of growing long bones. If one examines a section of the end of a normal long, growing bone (Fig. 647), a straight line may be seen where the white epiphyseal cartilage is joined to the cancellous shaft. The new bone is formed by a pushing of the medullary tissue from the cancellous bone into the epiphyseal cartilage. The two are joined by a straight, blue, semitranslucent band about 1 mm. broad, that is made up of hyperplastic cartilage, called the zone of growing cartilage.

Microscopical examination shows that in this area the cartilage cells have become greatly increased and are arranged in columns running parallel with the long axis of the bone. After these columns have acquired a certain height, there occurs at their base a deposition of calcareous material, which marks the cessation of the growth of cartilage. In a short time this calcified cartilage is destroyed by the pushing upward of the neighboring medullary tissue. These "buds" of medullary tissue, consisting of growing blood-vessels surrounded by a thin layer of medullary cells, push up between the columns of cartilage cells, gradually "eating" away the calcified, cartilaginous ground substance. The cartilage cells eventually disappear and are probably converted into medullary cells. Thus there are formed primary medullary canals bounded by the remains of the calcified cartilaginous ground substance, and it is this latter which then becomes converted into bone. This is brought about by the deposition within this substance of cells from the medullary canal which

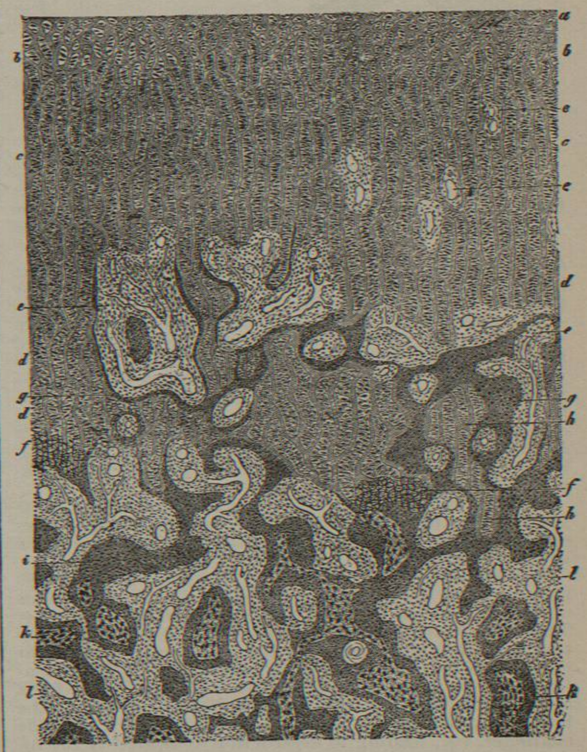

Fig. 648.—Longitudinal Section of the Line of Ossification in the Femur of a One-Year-Old Child Suffering from Rickets. (After Ziegler.) *a*, Hyaline cartilage; *b*, cartilage in the first stage of hyperplasia; *c*, zone of the columns of cartilage cells; *d*, columns of enlarged cells; *e*, vascularized marrow extending into the cartilage zone; *f*, calcified cartilage; *g*, osteoid tissue; *h*, remains of cartilage; *i*, columns of osteoid tissues; *k*, columns of osteoid uncalcified tissue, surrounded by true bone; *l*, vascular marrow tissue. (× 37 diameters.)

go to form the osteoblasts. The cartilage has formed the framework on which the growing bone has climbed, and is itself eventually absorbed.

In rachitic bone, the blue transition zone of hyperplastic cartilage is much wider, while its outline, both